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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,439	06/19/2001	Cornelius F. Ivory	WSUR117329	3241

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EXAMINER	
BARTON, JEFFREY THOMAS	

ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/885,439	IVORY ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Barton	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8,17,47-51,58,63 and 69-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,17,47-51,58,63 and 69-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050627*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 27 June 2005 has been entered.

Status of Objections and Rejections Pending Since the Office Action of 10 March 2005

2. The objection to claims 58, 63, and 69 is withdrawn due to Applicant's amendment.

3. The rejections made under the judicially created doctrine of obviousness-type double patenting are obviated by the filing of a terminal disclaimer over U.S. Patent No. 6,277,258.

4. The rejection of claims 1-3, 8, 17, 47-51, 63, and 69-71 under 35 U.S.C. §102(b) as anticipated by Koegler et al is withdrawn due to Applicant's amendment.

5. All other rejections are maintained.

Terminal Disclaimer

6. The terminal disclaimer filed on 27 June 2005 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,277,258 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 103

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1-3, 8, 17, 47-51, 63, and 69-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koegler et al. (*Biotechnol. Prog.* 1996)

Regarding claims 1 and 70, Koegler et al disclose a device for focusing charged solute (Figure 7), comprising: a first chamber for receiving a liquid medium (Inside the dialysis tubing) having an inlet and outlet for fluid flow into and out of the chamber (Indicated by arrows "Buffer and Protein" and "To Detector & Collection"); a second chamber (Outside the dialysis tubing) comprising an electrode array (Two electrodes is a plurality, see definition in specification Page 7, line 33 - Page 8, line 1; also see Future Directions section) having an inlet and outlet for fluid flow into and out of the chamber (Indicated by arrows, Recirculating Electrolyte (& Cooling)); a porous material separating the first and second chambers (dialysis tubing, Equipment section, 1st

paragraph); and suggests modification to include means for dynamically controlling the voltage applied to the electrode array to produce a dynamically shaped electric field. (Future Directions section)

Regarding claim 2, Koegler et al disclose the first and second chambers being in liquid communication. (Dialysis tubing allows aqueous liquid flow)

Regarding claim 3, Koegler et al disclose the first chamber being in electrical communication with the electrode array. (Figure 2 and caption)

Regarding claim 8, Koegler et al disclose the electrode array generating an electric field gradient profile. (Figure 2)

Regarding claim 17, Koegler et al disclose the device comprising first and second conduits for introducing and exiting fluid media from the first chamber. (Figure 7, indicated by arrows; details in 2nd - 4th paragraphs of Equipment section)

Regarding claims 47 and 71, Koegler et al disclose a method for focusing a charged solute in a fluid medium comprising: introducing a charged solute into a fluid medium, wherein the fluid medium is contained in a device according to claim 1 (Experiments section, 1st - 4th paragraphs); and applying an electric field gradient to the charged solute in the fluid medium to cause the charged solute to focus in a region of the medium. (Experiments section, 3rd and 4th paragraphs)

Regarding claim 48, Koegler et al disclose the first liquid being a buffer. (Experiments section, 3rd paragraph). They also refer to the flow of this buffer as elution. (5th paragraph)

Regarding claim 49, Koegler et al disclose the second liquid being a coolant buffer (Figure 7, arrow label)

Regarding claims 50 and 51, Koegler et al disclose the first liquid being either the same or different from the second liquid. (Experiments section, 2nd paragraph; describe buffer mismatch and contrast corresponding results to results without the mismatch (i.e. identical buffers))

Regarding claims 63 and 69, Koegler et al disclose a method for focusing a charged solute or separating charged solutes comprising: applying a charged solute to a fluid medium; applying a hydrodynamic force to the solute in the fluid medium; and opposing the hydrodynamic force with an electric field gradient to provide solutes focused in the fluid medium in order of their electrophoretic mobilities (All in Separation of Myoglobins section, 2nd paragraph); wherein the electric field gradient is generated by an electrode array (Figure 7; Future Directions section), and suggest dynamic control of the electric field gradient. (Future Directions section) They also disclose focusing and separation of proteins. (Separation of Myoglobins section)

Koegler et al do not explicitly disclose a device structure or methods of using a device wherein a dynamically shaped local field is produced.

However, in the "Future Directions" section of the reference, they provide an explicit suggestion to modify their system along the exact lines instantly claimed. They state, ". . . it is possible to manipulate the electric field gradient from outside the column by using a plurality of independent electrodes instead of the shaped chamber described in this paper. This allows the possibility that the field could be dynamically 'shaped'

during a run to improve performance." This reads on the limitations to "dynamically controlling the voltage" and "a dynamically-shaped field" in the instant claims. Although no illustration of such modification is provided, since this suggestion is for a limited modification to a device that is fully described in the reference, the Examiner considers this disclosure to sufficiently enable one having ordinary skill in the art to make and use the modified system.

9. Claims 4, 5, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koegler et al (*Biotechnol. Prog.* 1996) in view of Ivory et al. (U.S. Patent No. 5,298,143)

Koegler et al disclose devices and methods as described above in addressing claim 1. Relevant to claim 58, they also disclose a method, which was discussed above in addressing claims 63 and 69, corresponding to most limitations to this claim. They also suggest modifications that read on the limitations related to dynamic control. Relevant to claim 5, they also disclose individual control of electrodes in their array. (Future Directions section, "independent electrodes")

Koegler et al do not explicitly disclose a device or method in which a plurality of electrodes is arranged linearly along an axis parallel to the direction of migration of the solute.

Ivory et al disclose a similar gradient focusing device (Figure 16), which uses a linear array of ring electrodes (422-424) arranged along an axis parallel to the direction of solute migration.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device and method of Koegler et al by incorporating an array of electrodes arranged linearly along the outside of the separation chamber, as taught by Ivory et al, because it would provide greater control of the electric field gradient, and Koegler et al suggested the use of such electrode arrays.

10. Claims 72, 74, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koegler et al (*Biotechnol. Prog.* 1996) in view of Ivory et al. (U.S. Patent No. 5,298,143)

Relevant to claim 72, Koegler et al disclose a system for focusing a solute, comprising: a device according to claim 1 (See paragraph 8 above); an analytical instrument (Spectrophotometer; Equipment section, 4th paragraph); and an interface intermediate the device and the analytical instrument (Rainin flangeless fittings, Equipment section, 4th paragraph)

Relevant to claim 76, Koegler et al disclose the analytical instrument being an optical detection device. (Spectrophotometer)

Koegler et al do not explicitly disclose the system comprising a controller comprising a plurality of controller units in communication with the electrode array (Claim 72), nor do they disclose the controllers dynamically monitoring and setting the voltage at each electrode in response to signals from an operator. (Claim 74)

Ivory et al disclose a similar gradient focusing device (Figure 16) which uses a controller comprising a plurality of controller units in communication with the electrode

array. (Column 8, line 55 - Column 9, line 53) Relevant to claim 74, they also disclose the controller dynamically monitoring and setting the voltage in response to signals from an operator. (Column 9, lines 26-31)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device and method of Koegler et al by using a controller with a plurality of controller units in communication with the electrodes, as taught by Ivory et al, because it would provide the independent electrode control described by Koegler et al. (Future Direction section)

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to provide a controller that dynamically monitors and sets the voltage in response to operator signals, as taught by Ivory et al, because it would provide convenient, precisely controlled device operation.

11. Claim 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over Koegler et al (*Biotechnol. Prog.* 1996) and Ivory et al. (U.S. Patent No. 5,298,143) as applied to claim 72 above, and further in view of Hurd. (U.S. patent No. 4,670,119)

Koegler et al and Ivory et al disclose a combined system as described above in addressing claim 72.

Neither Koegler et al nor Ivory et al disclose a third chamber with a second electrode array and fluid inlets and outlets, separated from the first chamber by a second porous material, wherein the first and second porous materials are on opposite sides of the first chamber, and electrodes in the two arrays form pairs.

Hurd discloses a similar focusing device (Figure 5), in which there are two electrode arrays (22) disposed in an electrolyte chamber (10) each array being separated from the separation chamber (20) by a porous membrane (24), with electrodes in the array forming pairs (Column 9, lines 64-67), with the porous membranes (24) being on opposite sides of the separation chamber.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined system of Koegler et al and Ivory et al by providing an electrode geometry (i.e. pairs opposite each other, separated from the separation channel by oppositely-disposed membranes) as taught by Hurd, because it would provide an electric field gradient uniform in the channel cross section without requiring varying chamber width. It would also have been obvious to separate the electrode arrays into different chambers, because it would allow simpler construction of longitudinal inlets and outlets to the separation channel, of the type disclosed by Koegler et al (Figure 7).

12. Claim 75 is rejected under 35 U.S.C. 103(a) as being unpatentable over Koegler et al (*Biotechnol. Prog.* 1996) and Ivory et al. (U.S. Patent No. 5,298,143) as applied to claim 72 above, and further in view of Arai.

Koegler et al and Ivory et al disclose a combined system as described above in addressing claim 72.

Neither Koegler et al nor Ivory et al disclose a controller that sets the voltage at each electrode in response to signals from an analytical instrument.

Arai discloses an electrophoretic device comprising a controller that provides voltages based on signals from analytical devices. (Column 5, line 21 - Column 6, line 22)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined system of Koegler et al and Ivory et al by providing a controller that provides voltage control in response to signals from analytical devices, as taught by Arai, because it would allow system operation with minimal requirements for operator input.

13. Claim 77 is rejected under 35 U.S.C. 103(a) as being unpatentable over Koegler et al (*Biotechnol. Prog.* 1996) and Ivory et al. (U.S. Patent No. 5,298,143) as applied to claim 72 above, and further in view of Cabilly et al.

Koegler et al and Ivory et al disclose a combined system as described above in addressing claim 72. Koegler et al also disclose monitoring the progress of a separation using images taken at different times during the operation. (Figure 8)

Neither Koegler et al nor Ivory et al disclose the use of a video camera as an analytical instrument.

Cabilly et al disclose an electrophoresis apparatus that uses a video camera to record results of separations. (Column 4, lines 42-45)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined system of Koegler et al and Ivory et al by recording the progress of a separation with a video camera, because it would give a full

record of the separation progress and provide continuous data of the kind reported by Koegler et al. (Figure 8)

Response to Arguments

14. Applicant's arguments filed 27 June 2005 have been fully considered but they are not persuasive.

In response to applicant's argument that a skilled artisan would not have been motivated to include the electrodes disclosed in Ivory et al (US 5,298,143) in the device of Koegler et al, because it would have resulted in smearing of the analytes, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

As described in the rejections given above, Koegler et al describe a field gradient focusing apparatus and methods for its use, and explicitly suggest a modification to their design such that an array of electrodes is used to dynamically control and shape the electric field. Ivory et al (US 5,298,143) describe a field gradient focusing device that uses such a linear array of ring electrodes to provide the electric field. The issue is not whether the specific electrodes taken from the device of Ivory et al would function in the specific device of Koegler et al. Because Koegler et al suggest using an electrode array, Ivory et al disclose a device that uses a linear array as claimed, and their devices operate on the same principles (i.e. balancing electrophoretic and hydrodynamic forces

to focus analytes), the Examiner must maintain that a skilled artisan who was familiar with both disclosures would have been motivated to use a linear array of ring electrodes, based on the suggestion of Koegler et al and the fact that such a linear array had been previously used in a related device. Alleviation of complications resulting from such modification must be considered to be a matter of routine optimization.

Regarding the attachments appended to Professor Ivory's declaration, the skepticism of certain others in the field, indicated in Attachment C, cannot be considered to prove the nonobviousness of the claimed invention, given the disclosure of Koegler et al described above. Regarding Attachment B, the Examiner certainly does not dispute Professor Ivory's status as one having substantial skill in this art, particularly in view of the fact that his group produced the bulk of art cited in this case.

Applicant's arguments did not address the combination of Koegler et al and Ivory et al cited in rejecting claims 72-77, which did not involve modification of the electrode array suggested by Koegler et al. Therefore, these rejections are maintained.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
23 August 2005

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